

1. (Canceled)

2. (Currently Amended) A compound of Formula I



or a pharmaceutically acceptable salt thereof, wherein:

D is -NH-C(O)-NH-,

A is of the formula: -L-(M-L¹)_q, where

L is substituted or unsubstituted phenyl bound directly to D,

L¹ is phenyl or a 5 to 6 membered hetaryl moiety substituted by at least one substituent, -C(O)R_x,

wherein the heteroatoms of said hetaryl moiety consist of nitrogen,

M is oxygen,

q is 1 and

B is a substituted or unsubstituted pyridyl group, a substituted or unsubstituted quinolinyl group or a substituted or unsubstituted isoquinolinyl group,

where B is substituted, L is substituted or L¹ is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and W_n, where n is 0-3;

R_x is NR_aR_b where R_a and R_b are,

- a) independently hydrogen, ~~or selected from the group consisting of~~ C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₃₋₁₀ cycloalkyl, C₂₋₁₀ alkenyl, C₁₋₁₀ alkenoyl, C₆₋₁₂ aryl, C₃₋₁₂ hetaryl which is a 5-12 carbon atom aromatic ring system of 1-3 rings, at least one of which is aromatic, in which 1-3 carbon atoms are replaced by ~~having 1-3~~ heteroatoms selected from O, N and S, 5-6 membered C₃₋₁₂ cycloalkyl having 0-3 heteroatoms selected from N, S and O, ~~C₇₋₂₄-aralkyl, C₇₋₂₄-alkaryl,~~ substituted C₁₋₁₀ alkyl, substituted C₁₋₁₀ alkoxy, substituted 5-6 membered C₃₋₁₀ cycloalkyl, having 0-3 heteroatoms selected from N, S and O, substituted C₆₋₁₂ aryl, substituted C₃₋₁₂ hetaryl which is a 5-12 carbon atom aromatic ring system of 1-3 rings, at least one of which is aromatic, in which 1-3 carbon atoms are replaced by ~~having 1-3~~ heteroatoms selected from N, S and O, ~~substituted C₇₋₂₄-aralkyl, substituted C₇₋₂₄-alkaryl,~~ where R_a and R_b are a substituted group, they are substituted by halogen up to per halo, hydroxy, C₁₋₁₀ alkyl, 5-6 membered C₃₋₁₂ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₃₋₁₂ hetaryl which is a 5-12 carbon atom aromatic ring system of 1-3 rings, at least one

of which is aromatic, in which 1-3 carbon atoms are replaced by having 1-3 heteroatoms selected from N, S and O, C₁₋₁₀ alkoxy, C₆₋₁₂ aryl, halo-substituted C₁₋₆ halo-substituted alkyl up to per halo alkyl, halo-substituted C₆₋₁₂ halo-substituted aryl up to per halo aryl, halo-substituted 5-6 membered C₃₋₁₂ halo-substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C₃₋₁₂ hetaryl which is a 5-12 carbon atom aromatic ring system of 1-3 rings, at least one of which is aromatic, in which 1-3 carbon atoms are replaced by heteroatoms selected from N, S and O, up to per halo hetaryl, halo substituted C₇₋₂₄-aralkyl up to per halo aralkyl, halo substituted C₇₋₂₄-alkaryl up to per halo alkaryl;

each W is independently selected from the group consisting of -CN, -CO₂R⁷, -C(O)NR⁷R⁷, -C(O)-R⁷, -NO₂, -OR⁷, -SR⁷, -NR⁷R⁷, -NR⁷C(O)OR⁷, -NR⁷C(O)R⁷, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₂-C₁₀ alkenyl, C₁-C₁₀ alkenoyl, C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₆-C₁₄ aryl, C₇-C₂₄-alkaryl, C₇-C₂₄-aralkyl, C₃₋₁₂ hetaryl which is a 5-12 carbon atom aromatic ring system of 1-3 rings, at least one of which is aromatic, in which 1-3 carbon atoms are replaced by having 1-3 heteroatoms selected from O, N and S, C₄-C₂₃-alkheteroaryl having 1-3 heteroatoms selected from O, N and S, substituted C₁-C₁₀ alkyl, substituted C₁-C₁₀ alkoxy, substituted C₂-C₁₀ alkenyl, substituted C₁-C₁₀ alkenoyl, substituted C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, N and S, substituted C₆-C₁₂ aryl ~~[[]]~~ or substituted C₃-C₁₂ hetaryl which is a 5-12 carbon atom aromatic ring system of 1-3 rings, at least one of which is aromatic, in which 1-3 carbon atoms are replaced by having 1-3 heteroatoms selected from O, N and S, substituted C₇-C₂₄-aralkyl, substituted C₇-C₂₄-alkaryl, and substituted C₄-C₂₃-alkheteroaryl having 1-3 heteroatoms selected from O, N and S;

where W is a substituted group, it is substituted by one or more substituents which are each, independently, -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -OR⁷, -SR⁷, -NR⁷R⁷, -NO₂, -NR⁷C(O)R⁷, -NR⁷C(O)OR⁷ or halogen,

each R⁷ is independently selected from H, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₂-C₁₀ alkenyl, C₁-C₁₀ alkenoyl, C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, S and N,

~~C₆-C₁₄ aryl, C₃-C₁₂ hetaryl which is a 5-12 carbon atom aromatic ring system of 1-3 rings, at least one of which is aromatic, in which 1-3 carbon atoms are replaced by having 1-3 heteroatoms selected from O, N and S, C₇-C₁₄ alkaryl, C₇-C₂₄ aralkyl, C₄-C₂₃ alkheteroaryl having 1-3 heteroatoms selected from O, N and S, up to per-halosubstituted C₃-C₁₂ hetaryl which is a 5-12 carbon atom aromatic ring system of 1-3 rings, at least one of which is aromatic, in which 1-3 carbon atoms are replaced by having 1-3 heteroatoms selected from O, N and S, up to per-halosubstituted C₁-C₁₀ alkyl, up to per-halosubstituted C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, N and S, or up to per-halosubstituted C₆-C₁₄ aryl, up to per-halosubstituted C₇-C₂₄ aralkyl, up to per-halosubstituted C₇-C₂₄ alkaryl, and up to per-halosubstituted C₄-C₂₃ alkheteroaryl; and~~

each Z ~~is independently selected from the group consisting of CN, CO₂R⁷, C(O)R⁷, C(O)NR⁷R⁷, NO₂, OR⁷, SR⁷, NR⁷R⁷, NR⁷C(O)OR⁷, NR⁷C(O)R⁷, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₂-C₁₀ alkenyl, C₁-C₁₀ alkenoyl, C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, N and S, C₆-C₁₄ aryl, C₃-C₁₃ hetaryl having 1-3 heteroatoms selected from O, N and S, C₇-C₂₄ alkaryl, C₇-C₂₄ aralkyl, C₄-C₂₃ alkheteroaryl having 1-3 heteroatoms selected from O, N and S, substituted C₁-C₁₀ alkyl, substituted C₁-C₁₀ alkoxy, substituted C₂-C₁₀ alkenyl, substituted C₁-C₁₀ alkenoyl, substituted C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, N and S, substituted C₆-C₁₄ aryl, substituted C₇-C₂₄ alkaryl, substituted C₇-C₂₄ aralkyl and substituted C₄-C₂₃ alkheteroaryl having 1-3 heteroatoms selected from O, N and S; wherein if Z is a substituted group, the one or more substituents are selected from the group consisting of CN, CO₂R⁷, COR⁷, C(O)NR⁷R⁷, OR⁷, SR⁷, NO₂, NR⁷R⁷, NR⁷C(O)R⁷, and NR⁷C(O)OR⁷.~~

3. (Previously Presented) A compound as in claim 2 wherein L' is phenyl or pyridinyl.
4. (Currently amended) A compound as in claim 2 wherein the cyclic structures of B and L bound directly to D are substituted in the ortho position by hydrogen ~~Hydrogen~~.
5. (Currently amended) A compound of claim 2 wherein B of Formula I is a substituted pyridyl, substituted quinolinyl or substituted isoquinolinyl group substituted 1 to 3 times by ~~± one or more substituents which are each, independently, selected from the group~~

~~consisting of~~ -CN, halogen, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, -OH, up to per halo substituted C₁-C₁₀ alkyl, up to per halo substituted C₁-C₁₀ alkoxy or phenyl substituted by halogen up to per halo.

6. (Canceled)

7. (Canceled)

8. (Canceled)

9. (Previously Presented) A compound of claim 2, wherein L¹ is phenyl, pyridinyl or pyrimidinyl.

10. (Previously Presented) A compound of claim 5, wherein L¹ is phenyl, pyridinyl or pyrimidinyl.

11. (Canceled)

12. (Currently amended) A compound of claim 2 wherein L¹ is additionally substituted 1 to 3 times by one or more substituents which are each, independently, ~~selected from the group consisting of~~ C₁-C₁₀ alkyl, up to per halo substituted C₁-C₁₀ alkyl, -CN, -OH, halogen, C₁-C₁₀ alkoxy or ~~and~~ up to per halo substituted C₁-C₁₀ alkoxy.

13. (Canceled)

14. (Currently amended) A compound of claim 10 wherein L¹ is additionally substituted 1 to 3 times by one or more substituents which are each, independently, ~~selected from the group consisting of~~ C₁-C₁₀ alkyl, up to per halo substituted C₁-C₁₀ alkyl, -CN, -OH, halogen, C₁-C₁₀ alkoxy and or up to per halo substituted C₁-C₁₀ alkoxy.

15. (Previously Presented) A compound of claim 2 wherein L¹ is substituted only by -C(O)R_x.

16. (Previously Presented) A compound of claim 2 wherein L¹ is substituted by -C(O)R_x wherein R_x is NR_aR_b and R_a and R_b are independently hydrogen or C₁ - C₁₀ alkyl.

17. (Previously presented) A compound of claim 3 wherein L^1 is substituted by $-C(O)R_x$, wherein R_x is NR_aR_b and R_a and R_b are independently hydrogen or $C_1 - C_{10}$ alkyl.

18. (Previously presented) A compound of claim 10 wherein L^1 is substituted by $-C(O)R_x$, wherein R_x is NR_aR_b and R_a and R_b are independently hydrogen or $C_1 - C_{10}$ alkyl.

19. (Canceled)

20. (Canceled)

21. (Canceled)

22. (Canceled)

23. (Canceled)

24. (Canceled)

25. (Currently Amended) A compound of claim 2 which is a pharmaceutically acceptable salt of a compound of formula I which is selected from the group consisting of

a) a basic salt of an organic acid or inorganic acid which is ~~basic salts of organic acids and inorganic acids selected from the group consisting of~~ hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methanesulfonic acid, trifluorosulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or ~~and~~ mandelic acid; and

b) ~~acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations~~ an acid salt of an organic or inorganic base containing a cation which is an alkaline cation, alkaline earth cation, the ammonium cation, an aliphatic substituted ammonium cation or an aromatic substituted ammonium cation.

26. (Canceled)

27. (Currently amended) A pharmaceutical composition comprising a compound of Formula I of claim 2 or a pharmaceutically acceptable salt of a compound of formula I, and a physiologically acceptable carrier.

28. (Canceled)

29. (Currently Amended) A method for inhibiting raf kinase in a host ~~the treatment of solid cancers~~ comprising administering to a host in need thereof an effective amount of a compound of Formula I of claim 2.

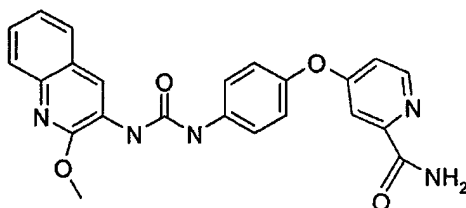
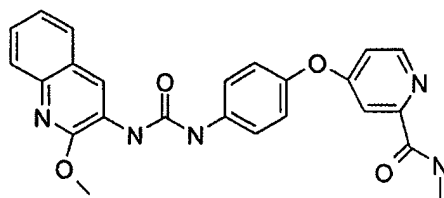
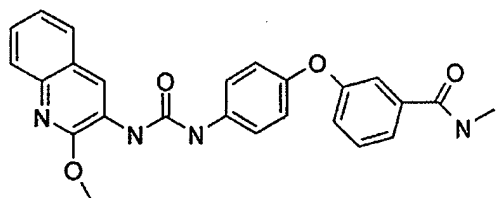
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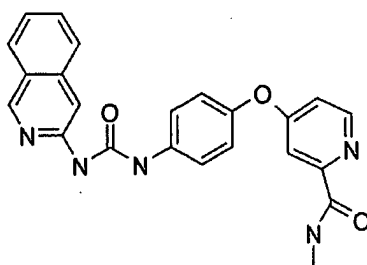
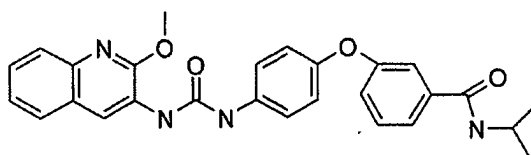
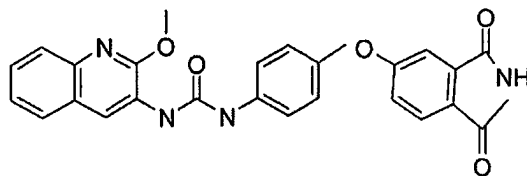
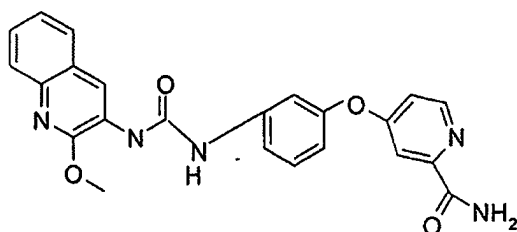
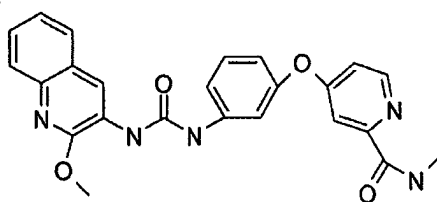
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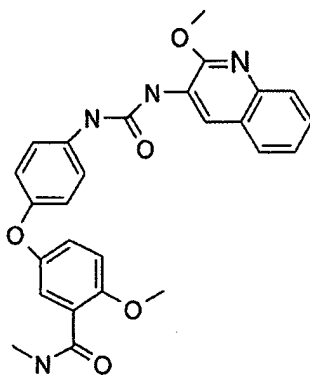
32. (Canceled)

33. (Canceled)

34. (Currently amended) A compound which is ~~selected from the group consisting of~~

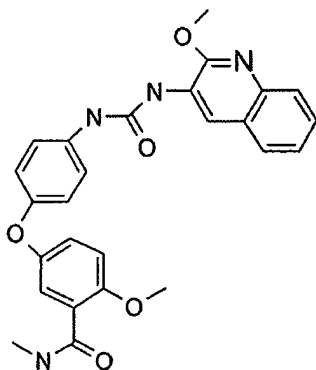
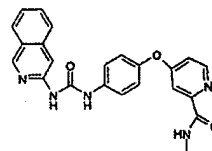
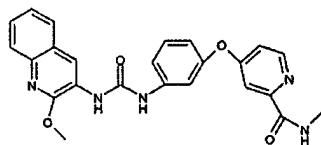
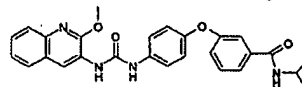
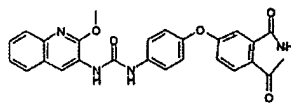
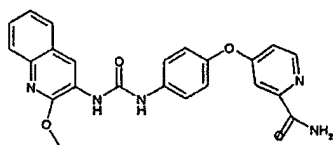
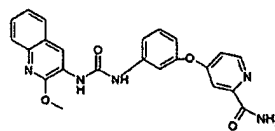
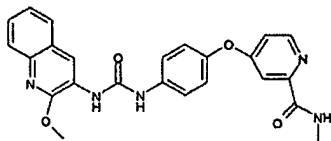
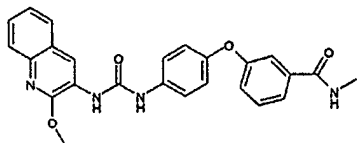






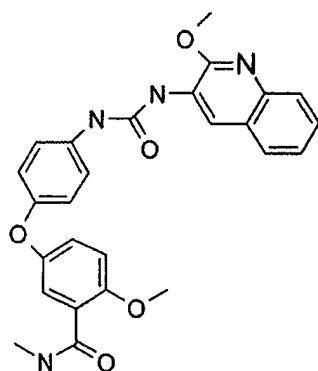
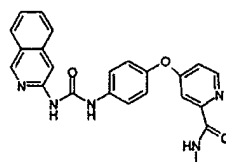
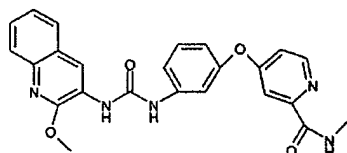
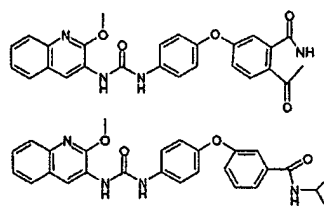
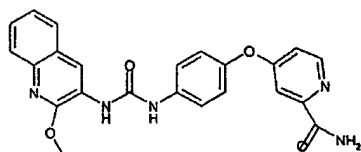
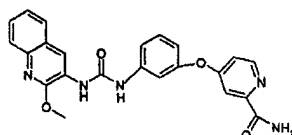
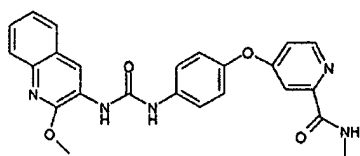
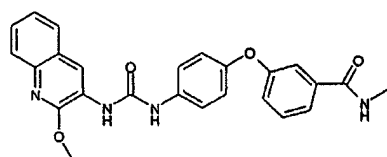
or a and pharmaceutically acceptable salts salt thereof.

35. (Previously presented) A pharmaceutical composition comprising a compound which is ~~selected from the group consisting of~~



or a ~~and their~~ pharmaceutically acceptable salt thereof salts, and a physiologically acceptable carrier.

36. (Currently amended) A method for inhibiting raf kinase in a host ~~the treatment of solid cancers~~, comprising administering to a host in need thereof an effective amount of a compound which is ~~selected from the group consisting of~~



or a and pharmaceutically acceptable salts salt thereof.

37. (Currently Amended) A compound of Formula I:

A - D - B (I)

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is of the formula: $-L-(M-L^1)_q$, where L is phenyl bound directly to D, L^1 is pyridinyl, M is oxygen and q is 1; and

B is a substituted or unsubstituted pyridyl, quinolinyl or isoquinolinyl group,

wherein L^1 is substituted by $-C(O)R_x$,

R_x is NR_aR_b where R_a and R_b are

independently hydrogen, C_1 - C_{10} alkyl, C_1 - C_{10} alkoxy, C_3 - C_{10} cycloalkyl, C_2 - C_{10} alkenyl, C_1 - C_{10} alkenoyl, C_6 - C_{12} aryl, C_3 - C_{12} hetaryl which is a 5-12 carbon atom aromatic ring system of 1-3 rings, at least one of which is aromatic, in which 1-3 carbon atoms are replaced by having 1-3 heteroatoms selected from O, N and S, 5-6 membered C_3 - C_{12} cycloalkyl having 0-3 heteroatoms selected from N, S and O, C_7 - C_{24} aralkyl, C_7 - C_{24} alkaryl, substituted C_1 - C_{10} alkyl, substituted C_1 - C_{10} alkoxy, substituted 5-6 membered C_3 - C_{10} cycloalkyl, having 0-3 heteroatoms selected from N, S and O, substituted C_6 - C_{12} aryl, substituted C_3 - C_{12} hetaryl which is a 5-12 carbon atom aromatic ring system of 1-3 rings, at least one of which is aromatic, in which 1-3 carbon atoms are replaced by having 1-3 heteroatoms selected from N, S and O, substituted C_7 - C_{24} aralkyl, substituted C_7 - C_{24} alkaryl, where R_a and R_b are a substituted group, they are substituted by halogen up to per halo, hydroxy[[7]] or C_1 - C_{10} alkyl; or

where B is substituted, L is substituted or L^1 is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and W_n , where n is 0-3;

wherein each W is independently selected from the group consisting of $-CN$, $-CO_2R^7$, $-C(O)NR^7R^7$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, C_1 - C_{10} alkyl, C_1 - C_{10} alkoxy, C_2 - C_{10} alkenyl, C_1 - C_{10} alkenoyl, C_3 - C_{10} cycloalkyl ~~having 0-3 heteroatoms selected from O, S and N, C_6 - C_{14} aryl, C_7 - C_{24} alkaryl, C_7 - C_{24} aralkyl, C_3 - C_{12} hetaryl which is a 5-12 carbon atom aromatic ring system of 1-3 rings, at least one of which is aromatic, in which 1-3 carbon atoms are replaced by having 1-3 heteroatoms selected from O, N and S, C_4 - C_{23} alkhetaroaryl having 1-3 heteroatoms selected from O, N and S, substituted C_1 - C_{10} alkyl, substituted C_1 - C_{10} alkoxy, substituted C_2 - C_{10} alkenyl, substituted C_1 - C_{10} alkenoyl, substituted C_2 - C_{10} cycloalkyl having 0-3 heteroatoms selected from O, N and S, substituted C_6 - C_{12} aryl, substituted C_3 - C_{12} hetaryl having 1-3 heteroatoms selected from O, N and S, substituted C_7 - C_{24} aralkyl, substituted C_7 - C_{24} alkaryl, and substituted C_4 - C_{23} alkhetaroaryl having 1-3 heteroatoms selected from O, N and S, optionally substituted by one~~

or more substituents which are, independently, selected from the group consisting of -CN, -CO₂R⁷, -C(O)R⁷, -C(O)NR⁷R⁷, -OR⁷, -SR⁷, -NR⁷R⁷, -NO₂, -NR⁷C(O)R⁷, -NR⁷C(O)OR⁷ and or halogen up to per-halo; with each R⁷ independently ~~selected from H, or C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₂-C₁₀ alkenyl, C₁-C₁₀ alkenoyl, C₃-C₁₀ cycloalkyl having 0-3 heteroatoms selected from O, S and N, C₆-C₁₄ aryl, C₃-₁₂ hetaryl which is a 5-12 carbon atom aromatic ring system of 1-3 rings, at least one of which is aromatic, in which 1-3 carbon atoms are replaced by~~ having 1-3 heteroatoms selected from O, N and S, C₇-C₁₄ alkaryl, C₇-C₂₄ aralkyl, C₄-C₂₃ alkheteroaryl having 1-3 heteroatoms selected from O, N and S, up to per-halosubstituted C₃-C₁₃ hetaryl which is a 5-12 carbon atom aromatic ring system of 1-3 rings, at least one of which is aromatic, in which 1-3 carbon atoms are replaced by having 1-3 heteroatoms selected from O, N and S, up to per-halosubstituted C₁-C₁₀ alkyl, up to per-halosubstituted C₃-C₁₀ cycloalkyl ~~having 0-3 heteroatoms selected from O, N and S, or~~ up to per-halosubstituted C₆-C₁₄ aryl, ~~up to per-halosubstituted C₇-C₂₄ aralkyl, up to per-halosubstituted C₇-C₂₄ alkaryl, and up to per-halosubstituted C₄-C₂₃ alkheteroaryl.~~

38. (Canceled)

39. (Previously Presented) A compound as in claim 37 wherein the cyclic structures of B and L bound directly to D are substituted in the ortho position by hydrogen.

40. (Currently amended) A compound of claim 37 wherein B of Formula I is a substituted pyridyl, substituted quinoliny or isoquinoliny group substituted 1 to 3 times by 1 or more substituents which are each independently ~~selected from the group consisting of~~ -CN, halogen, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, -OH, up to per halo substituted C₁-C₁₀ alkyl, up to per halo substituted C₁-C₁₀ alkoxy or phenyl substituted by halogen up to per halo.

41. (Canceled)

42. (Currently amended) A compound of claim 37 wherein L¹ is additionally substituted 1 to 3 times by one or more substituents which are each, independently, selected from the ~~group consisting of~~ C₁-C₁₀ alkyl, up to per halo substituted C₁-C₁₀ alkyl, -CN, -OH, halogen, C₁-C₁₀ alkoxy ~~and~~ or up to per halo substituted C₁-C₁₀ alkoxy.

43 (Canceled)

44, (Canceled)

45. (Currently amended) A compound as in claim 37 wherein substituents for B and L and additional substituents for L¹, are each, independently, ~~selected from the group consisting of C₁-C₁₀ alkyl up to per halo substituted C₁-C₁₀ alkyl, CN, OH, halogen, C₁-C₁₀ alkoxy and or up to per halo substituent substituted C₁-C₁₀ alkoxy.~~

46. (Currently amended) A compound of claim 37 which is a pharmaceutically acceptable salt of a compound of formula I which is ~~selected from the group consisting of~~

a) ~~basic salts of organic acids and inorganic acids selected from the group consisting of~~ a basic salt of an organic acid or inorganic acid which is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluorosulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-naphthalene sulfonic acid, 2-naphthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, ~~and or~~ mandelic acid; and

b) ~~acid salts of organic and inorganic bases containing cations selected from the group consisting of alkaline cations, alkaline earth cations, the ammonium cation, aliphatic substituted ammonium cations and aromatic substituted ammonium cations~~ an acid salt of an organic or inorganic base containing a cation which is an alkaline cation, alkaline earth cation, the ammonium cation, an aliphatic substituted ammonium cation or an aromatic substituted ammonium cation.

47. (Previously presented) A pharmaceutical composition comprising a compound of claim 37 or a pharmaceutically acceptable salt of a compound of formula I, and a physiologically acceptable carrier.

48. (Currently amended) A method of inhibiting raf kinase in a host ~~for the treatment of solid cancers,~~ comprising administering to a host in need thereof an effective amount of a compound of Formula I of claim 37.

49. (Currently amended) A compound as in claim 37 wherein R_x is NR_aR_b and R_a and R_b are each, independently, ~~selected from~~ hydrogen and or $C_1 - C_{10}$ alkyl.